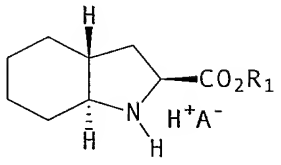
Claims:

1. A method for the synthesis of a compound of formula I as a mixture of enantiomers,



(I)

(wherein $R_1$ is H or an acid protective group and $H^+A^-$ indicates an optional acid with which the compound of formula I may form an ammonium salt)

said method comprising;

A) reacting a cyclohexyl aziridine with a dialkyl malonate, whereby to provide a trans-fused 3-alkylcarbonyl-octahydro-indol-2-one;

B) decarbonylation at the 3-position, conversion of the ketone of the resulting trans-octahydro-indol-2-one to an optionally protected carboxylic acid group; and

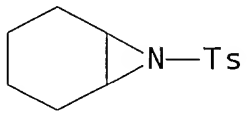
C) optionally removing any N-substitution if necessary.

2. A method as claimed in claim 1 wherein said mixture of enantiomers consists of more than 50:50 (2S, 3aR, 7aS):(2R, 3aS, 7aR).

3. A method as claimed in claim 2 wherein step A and/or step B is carried out in the presence of a chiral auxiliary.

4. A method as claimed in any one of claims 1 to 3

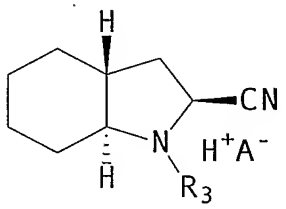
wherein said cyclohexyl aziridine is




5. A method as claimed in any one of claims 1 to 4 wherein said dialkylmalonate is diethylmalonate.

6. A method as claimed in any one of claims 1 to 5 wherein decarbonylation is carried out by heating said trans-fused 3-alkylcarbonyl-octahydro-indol-2-one in the presence of a halide salt and subsequently hydrolysing.

7. A method as claimed in any of claims 1 to 6 wherein conversion of said ketone to an optionally protected carboxylic acid comprises the reduction of said ketone to an alcohol moiety, followed by the stereoselective conversion of said alcohol moiety to a nitrile compound of formula II, followed by conversion of said nitrile compound to an optionally protected carboxylic acid;




(II)

wherein $H^+A^-$ are as defined in claim 1 and $R_3$ is H or a leaving group.

8. A method as claimed in claim 7 wherein said stereoselective conversion of said alcohol moiety to a nitrile compound of formula II is carried out in the presence of a metal halide.

9. A method as claimed in claim 8 wherein said metal halide is tin tetrachloride, titanium tetrachloride or iron trichloride.

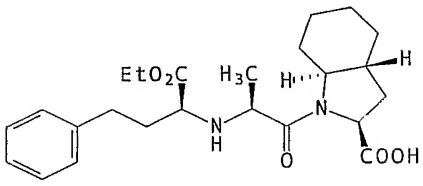
10. A method for the formation of a compound of formula III comprising forming a compound of formula I by a method as claimed in any of claims 1 to 9 followed by;

i) amide formation with an activated acid of formula IV or V;

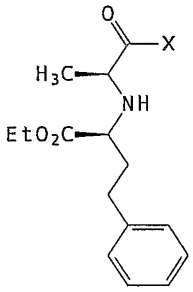
ii) separation of enantiomers by conversion to diastereoisomers and separation thereof;

iii) removal of any protecting group at $R_1$ such that $R_1$ is hydrogen;

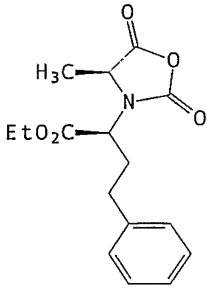
wherein steps i) to iii) may be carried out in any order and the conversion to diastereoisomers in step ii) may be by means of the amide formation of step i);




(III)




(IV)




(V)

wherein X is OH or an acid activating group.

11. A method as claimed in claim 10 wherein the protecting group at $R_1$, if present, is a benzyl group.

12. A method as claimed in any one of claims 10 to 11

wherein diastereomer separation is carried out via reaction with O,O'-dibenzoyl-L-tartaric acid.

13. A method as claimed in any one of claims 10 to 12 wherein the steps are carried out in the order (i), (iii) and (ii).

14. A method as claimed in any one of claims 10 to 12 wherein the steps are carried out in the order (ii), (i) and (iii).

15. An intermediate of formula I as defined in claim 1, formed by a method as claimed in any of claims 1 to 9.

16. An intermediate of formula II as defined in claim 7, formed by a method as claimed in claim 7 to 9.

17. Trandolapril having formula III as defined in claim 10 formed by a method as claimed in claim 10 to 14.